Fundamental Research 3 (2023) 655–656

Contents lists available at ScienceDirect

Fundamental Research

journal homepage: http://www.keaipublishing.com/en/journals/fundamental-research/

Editorial

RNA biology and therapeutics

Puyue Wang[a], Yuanchao Xue[b,c], Yijun Qi[d,e,*], Runsheng Chen[b,c,*]

[a] Department of Life Sciences, National Natural Science Foundation of China, Beijing 100085, China
[b] Key Laboratory of RNA Biology, Institute of Biophysics, Chinese Academy of Sciences, Beijing 100101, China
[c] University of Chinese Academy of Sciences, Beijing 100049, China
[d] Center for Plant Biology, School of Life Sciences, Tsinghua University, Beijing 100084, China
[e] Tsinghua University-Peking University Joint Center for Life Sciences, School of Life Sciences, Tsinghua University, Beijing 100084, China

Eukaryotic genomes undergo pervasive transcription, generating vast amounts of noncoding RNAs alongside protein-coding mRNAs [1]. These noncoding RNAs, including small noncoding RNAs, long noncoding RNAs (lncRNAs), and circular RNAs, have been shown to play critical roles in gene regulation, chromatin remodeling, assembly of membraneless organelles, and other essential biological processes. They function through a diverse range of mechanisms [2–5]. Dysregulation of noncoding RNAs contributes to human disease pathogenesis and affects plant development and stress response [6–8]. Over the past decade, significant progress has been made in unraveling the functions of noncoding RNAs and elucidating the molecular mechanisms by which they operate. The involvement of noncoding RNAs in human disease pathogenesis and agronomic trait regulation has garnered increasing attention.

RNA molecules can fold into secondary and tertiary structures via Watson–Crick, Hoogsteen, or wobble base pairing [9]. The functions of many regulatory RNAs depend on the formation of these structures and their ability to adapt to cellular conditions [10]. Mutations that disrupt RNA structures are associated with various human diseases, including neurodegenerative diseases [11]. However, determining and modeling RNA structures, particularly tertiary structures, remains a significant challenge due to their inherent flexibility.

RNA molecules undergo modifications by various chemical groups, with over 160 types of RNA modifications currently identified [12]. Investigation into several abundant RNA modifications has revealed that RNA modifications, such as the internal mRNA modification *N*6-methyladenosine (m6A), regulate RNA metabolism and are involved in various cellular, developmental, and disease processes [13–15]. In recent years, efforts have been made to develop high-throughput methods for profiling different RNA modifications, especially non-abundant ones. Such efforts have enabled the identification of writers, readers, and erasers, thereby broadening our understanding of the diverse biological roles played by various RNA modifications.

Our growing understanding of the functions of different types of RNAs and their crucial roles in pathogenesis promotes the rise and development of RNA-based therapeutics. They have the potential to revolutionize future disease treatment as they can target proteins, transcripts, or genes that are beyond the reach of conventional drugs. RNA-based therapeutics can be based on mRNA, antisense RNA, RNA interference (RNAi), and RNA aptamers [16]. In the early 2010s, RNA-based cancer therapy had significant progress [17]. This success continued with the development of mRNA vaccines targeting SARS-CoV-2, which have proven to be highly effective in saving numerous lives [18]. However, there are still many RNA-based therapeutics under development that have not been used clinically. The main challenges in this field include improving RNA metabolic stability, enhancing the efficiency and specificity of RNA delivery, and attaining minimal immunogenicity.

This special issue of *Fundamental Research* focuses on RNA biology and therapeutics, presenting a collection of one perspective, nine review articles, and one original research article. Zou et al. [19] bring to our attention new regulatory functions of RNA, while Yin et al. [20] review the functions and mechanisms of chromatin-bound RNAs. Gou et al. [21], Liu et al. [22], and Zhu et al. [23] discuss the contribution of dysregulated noncoding RNAs to human diseases, including tumorigenesis and inflammation. In their review, Xu et al. [24] explore miRNA biogenesis pathways in plants, and Zhang et al. [25] summarize the roles of noncoding RNAs in regulating agronomic traits. Shu et al. [26] introduce a new technique, a^{6}A-seq, which allows for the examination of RNA dynamics. Deng et al. [27] review the technical advances in RNA structural analysis, while Li et al. [28] cover the role of mRNA modifications and advancements in mRNA modification detection. Finally, Wei et al. [29] provide a comprehensive review of the current status of mRNA-based therapeutics, discussing potential future directions for improvement. These articles offer valuable insights and are expected to inspire further research in the exciting fields of RNA biology and RNA-based therapeutics.

References

[1] X. Li, X.D. Fu, Chromatin-associated RNAs as facilitators of functional genomic interactions, Nat. Rev. Genet. 20 (2019) 503–519.
[2] K. Palos, L. Yu, C.E. Railey, A.C. Nelson Dittrich, A.D.L Nelson, Linking discoveries, mechanisms, and technologies to develop a clearer perspective on plant long noncoding RNAs, Plant Cell 35 (2023) 1762–1786.
[3] A.T. Wierzbicki, T. Blevins, S. Swiezewski, Long noncoding RNAs in plants, Annu. Rev. Plant Biol. 72 (2021) 245–271.
[4] L. Statello, C.J. Guo, L.L. Chen, M. Huarte, Gene regulation by long non-coding RNAs and its biological functions, Nat. Rev. Mol. Cell Biol. 22 (2021) 96–118.

* Corresponding authors.
E-mail addresses: qiyijun@tsinghua.edu.cn (Y. Qi), rschen@ibp.ac.cn (R. Chen).

https://doi.org/10.1016/j.fmre.2023.07.001

[5] X. Fang, Y. Qi, RNAi in plants: an argonaute-centered view, Plant Cell 28 (2016) 272–285.
[6] Y. Yu, Y. Zhang, X. Chen, Y. Chen, Plant noncoding RNAs: hidden players in development and stress responses, Annu. Rev. Cell Dev. Biol. 35 (2019) 407–431.
[7] M. Esteller, Non-coding RNAs in human disease, Nat. Rev. Genet. 12 (2011) 861–874.
[8] X. Song, Y. Li, X. Cao, Y. Qi, MicroRNAs and their regulatory roles in plant-environment interactions, Annu. Rev. Plant Biol. 70 (2019) 489–525.
[9] K.M. Weeks, Advances in RNA structure analysis by chemical probing, Curr. Opin. Struct. Biol. 20 (2010) 295–304.
[10] L.R. Ganser, M.L. Kelly, D. Herschlag, H.M. Al-Hashimi, The roles of structural dynamics in the cellular functions of RNAs, Nat. Rev. Mol. Cell Biol. 20 (2019) 474–489.
[11] V. Bernat, M.D. Disney, RNA structures as mediators of neurological diseases and as drug targets, Neuron 87 (2015) 28–46.
[12] G. Huang, Q. Ding, D. Xie, Z. Cai, Z. Zhao, Technical challenges in defining RNA modifications, Semin. Cell Dev. Biol. 127 (2022) 155–165.
[13] W.V. Gilbert, S. Nachtergaele, mRNA regulation by RNA modifications, Annu. Rev. Biochem. 92 (2023) 175–198.
[14] N. Jonkhout, J. Tran, M.A. Smith, N. Schonrock, J.S. Mattick, E.M. Novoa, The RNA modification landscape in human disease, RNA 23 (2017) 1754–1769.
[15] P.C. He, C. He, m(6) A RNA methylation: from mechanisms to therapeutic potential, EMBO J. 40 (2021) e105977.
[16] Y. Zhu, L. Zhu, X. Wang, H. Jin, RNA-based therapeutics: an overview and prospectus, Cell Death. Dis. 13 (2022) 644.
[17] U. Sahin, K. Kariko, O. Tureci, mRNA-based therapeutics–developing a new class of drugs, Nat. Rev. Drug Discov. 13 (2014) 759–780.
[18] O.J. Watson, G. Barnsley, J. Toor, A.B. Hogan, P. Winskill, A.C. Ghani, Global impact of the first year of COVID-19 vaccination: a mathematical modelling study, Lancet Infect. Dis. 22 (2022) 1293–1302.
[19] Z. Zou, J. Wei, C. He, New horizons of regulatory RNA, Fund. Res. 3 (5) (2023) 760–762.
[20] Y. Yin, X. Shen, Noncoding RNA-chromatin association: Functions and mechanisms, Fund. Res. 3 (5) (2023) 665–675.
[21] L.-T. Gou, Q. Zhu, M.-F. Liu, Small RNAs: An expanding world with therapeutic promises, Fund. Res. 3 (5) (2023) 676–682.
[22] J. Liu, F. Zhao, L.-L. Chen, S. Su, Dysregulation of circular RNAs in inflammation and cancers, Fund. Res. 3 (5) (2023) 683–691.
[23] P. Zhu, B. Liu, Z. Fan, Noncoding RNAs in tumorigenesis and tumor therapy, Fund. Res. 3 (5) (2023) 692–706.
[24] Y. Xu, X. Chen, microRNA biogenesis and stabilization in plants, Fund. Res. 3 (5) (2023) 707–717.
[25] Y.-C. Zhang, C. Yuan, Y.-Q. Chen, Noncoding RNAs and their roles in regulating the agronomic traits of crops, Fund. Res. 3 (5) (2023) 718–726.
[26] X. Shu, C. Huang, T. Li, et al., a6A-seq: N6-allyladenosine-based cellular messenger RNA metabolic labelling and sequencing, Fund. Res. 3 (5) (2023) 657–664.
[27] J. Deng, X. Fang, L. Huang, et al., RNA structure determination: From 2D to 3D, Fund. Res. 3 (5) (2023) 727–737.
[28] K. Li, J. Peng, C. Yi, Sequencing methods and functional decoding of mRNA modifications, Fund. Res. 3 (5) (2023) 737–748.
[29] H.-H. Wei, L. Zheng, Z. Wang, mRNA therapeutics: New vaccination and beyond, Fund. Res. 3 (5) (2023) 749–760.

Puyue Wang is a professor and the Director in the Division of Biomedicine, Department of Life Sciences, National Natural Science Foundation of China. She completed a Ph.D. degree in Cell and Developmental Biology at University of Pennsylvania in 2007.

Yijun Qi is a professor in the School of Life Sciences and Center for Plant Biology at Tsinghua University in Beijing. He completed a Ph.D. in Plant Virology at Zhejiang University. He is an expert on noncoding RNAs in plants. Work in his laboratory includes identification of new types of small RNAs and investigating the mechanisms of small RNA biogenesis and action in plants and the functions of small RNAs in regulating agronomic traits in crops. He has won a number of prestigious awards including National Innovation Award, National Science and Technology Award (the Second Prize), National Youth Science and Technology Award, and Tan Jia-Zhen Life Science Innovation Award.

Runsheng Chen is an investigator at the Institute of Biophysics, CAS. His research interests include theoretical biology, bioinformatics and noncoding RNAs. He is a Member of the Chinese Academy of Sciences and the International Eurasian Academy of Sciences. He has won a number of prestigious awards including Ho Leung Ho Lee Prize, Tan Jia-Zhen Life Science Achievement Award and National Science and Technology Advancement Award (the Second Prize).